Respiratory Syncytial Virus Vaccine (MRESVIA)
Mini-Monograph
August 2024

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The purpose of VA National Formulary Committee drug monographs is to provide a focused drug review for making formulary decisions. The Product Information or other resources should be consulted for detailed and most current drug information.

FDA Approval	**Description/MOA**	MRESVIA is a modified mRNA RSV vaccine (containing pre-F RSV glycoprotein) which works by inducing an immune response against RSV
	Indication(s) Under Review	Prevention of lower respiratory tract disease caused by respiratory syncytial virus in individuals 60 years of age and older. Approved by FDA on 5/31/24
	Dosage Form(s)	Supplied as a single-dose prefilled syringe with frozen suspension to be thawed prior to administration

Clinical Evidence	**Study/Design**	One large phase 2/3 trial (ConquerRSV**)** in patients ≥ 60 years of age who received MRESVIA (n=17,734) or placebo (n=17,679). **Primary endpoints were vaccine efficacy (VE) for RSV-LRTD* with 2 or with 3 symptoms comparing IR/1000 PY with vaccine vs. placebo at least 14 days to 12 months after vaccination.** Other endpoints included RSV-LRTD by subtype and hospitalization. Smaller supportive trials assessed immunogenicity, safety and immune persistence
	Population	**Conquer RSV** enrolled immunocompetent patients (healthy or with stable chronic conditions) aged ≥60 years. Clinically unstable comorbidities, immunocompromise and history of myocarditis or pericarditis within 2 months prior to screening were exclusions.
	Demographics	Median age 67 years; male (51%); race (63% white, 12% black, 9% Asian) Participants were followed for a median of 3.7 month for the primary outcome. Additional analysis at a median follow-up of 8.6 months was also reported. 30% had at least 1 comorbidity (COPD, asthma, chronic respiratory disease, CHF, advanced liver disease or advanced kidney disease)
	Intervention	Single intramuscular dose vs. placebo (0.5 mL)
	Results	MRESVIA VE for RSV-associated LRTD with ≥ 2 symptoms was 79% (15 vs. 70 cases) and ≥ 3 symptoms was 81% (5 vs. 26 cases) with 3.7 months median follow-up. (Primary endpoint) After an additional 8.6 months median follow up, VE was 63% for RSV-LRTD with ≥2 or 61% with ≥3 symptoms. At latest follow-up (median 18.8 months) efficacy was 47% and 48% against RSV-LRTD with 2 or 3 sx. Too few hospitalizations occurred to assess VE for this endpoint Significant benefit also shown in subgroups (age 60-69 yrs., 70-79 yrs., those with ≥ 1 comorbidity)
	Limitations	Low number of cases, short follow-up to assess immune-persistence in subsequent years Low number of patients at highest risk for RSV complications and low numbers of hospitalizations during trial. Efficacy in higher risk patients unknown
	Summary	A single dose of MRESVIA provided moderate to high efficacy in reducing RSV-LRTD but benefit on hospitalization or death or benefit in highest risk populations are unknown.

**RSV-LRTD: at least 2 or 3 signs or symptoms (shortness of breath, cough and/or fever, wheezing and/or rales and/or rhonchi, sputum production, tachypnea, hypoxemia, or pleuritic chest pain) lasting > 1 day with PCR confirmed RSV.*

Abbreviations: MOA=mechanism of action; RSV=respiratory syncytial virus; n=number of patients; IR/1000PY=Incidence rate per 1000 person years; RSV-LRTD= RSV confirmed lower respiratory tract infection; TBD=to be determined; VANF=VA National Formulary; GBS=Guillain-Barre syndrome

Safety	**Boxed Warnings**	None
	Contraindications	History of severe allergic reaction to any component of the MRESVIA
	Warnings/ Precautions	Prevention and management of allergic reactions, syncope (after administration) Those who are immunocompromised may have a diminished response
	Adverse reactions (AE)	**Solicited AEs in ConquerRSV (MRESVIA vs. placebo):** • **Injection site pain (56% vs. 14%)** • Fatigue (31% vs. 20%) • Myalgia (26% vs. 14%) • Headache (27% vs. 19%) • Arthralgia (22% vs. 14%) **Serious AEs (SAEs) in 8% of each group** • 1 case of facial paralysis related to MRESVIA occurred 4 days after vaccination. No other notable patterns (including Bell's palsy) were noted between the groups. o 3 cases of GBS* (1 vaccine, 2 placebo) but all were > 500 days after vaccination • No cases of myocarditis or pericarditis within 42 days

**GBS = Guillain Barre syndrome*

Alternatives	Formulary status	Clinical Guidance	Other Considerations
RSV vaccine, mRNA (MRESVIA)	TBD	FDA approved for patients aged 60 years and older as a single dose ACIP recommended for ≥ 75 years of age or 60-74 years of age with one or more risk factors for severe RSV	Adverse events similar to mRNA COVID-19 vaccines. Indirectly AE's may be higher than ABRYSVO vast majority mild-moderate Very few neuroinflammatory AEs
RSV vaccine, adjuvanted (ABRYSVO)	F	FDA approved for patients aged 60 years and older as a single dose ACIP recommended for ≥ 75 years of age or 60-74 years of age with one or more risk factors for severe RSV	Compared with placebo local and systemic AEs may be slightly lower than other two vaccines Possible imbalance in GBS cases vs. AREXVY in some f/u data from ACIP but not all follow-up real-world analyses
RSV vaccine, adjuvanted (AREXVY)	F	FDA approved for patients aged 60 years and older as a single dose ACIP recommended for ≥ 75 years of age or 60-74 years of age with one or more risk factors for severe RSV	Adverse events may be higher than ABRYSVO, possibly due to adjuvant but most mild-moderate and no head to head data

Conclusions/Projected Place in Therapy

- RSV is associated with an estimated 90,000-140,000 hospitalizations annually in adults aged 65 years and older. Certain conditions, increase the risk for severe disease and hospitalization.

- MRESVIA demonstrated moderate to high efficacy reducing the incidence of RSV-LRTD in adults aged 60 years or older; clinical trials thus far have not been powered to show a difference in RSV requiring hospitalization or death. In addition, those at highest risk (multiple comorbidities, immunocompromised, frail) were not included or underrepresented in the phase 2/3 trial, so efficacy in those populations is unclear.

- **In June of 2024, the ACIP voted to recommend that adults ≥ 75 years and those 60-74 years with risk factors for severe RSV receive a single dose of an RSV vaccine.** This was a change from the 2023 recommendations that RSV vaccine be administered to those ≥ 60 years using shared decision-making.

- Risk factors for severe RSV included by ACIP are listed below
    - Chronic lung disease (asthma, COPD, interstitial lung disease)
    - Chronic cardiovascular disease (e.g., CHF or coronary artery disease, excluding isolated hypertension)
    - Moderate/severe immunocompromise
    - Diabetes mellitus **with end organ damage (e.g., neuropathy, retinopathy or requiring insulin or sodium-glucose cotransporter-2 (SGLT2) inhibitor**
    - Neurologic or neuromuscular condition that impairs airway clearance or causes respiratory muscle weakness (e.g., poststroke aphasia, amyotrophic lateral sclerosis)
    - Advanced chronic kidney disease or liver disease (e.g., cirrhosis)
    - Hematologic disorders (such as sickle cell disease or thalassemia)
    - **Severe** obesity (body mass-index ≥ 40 kg/m^2)
    - Other factors include
        - Residence in a nursing home or other long-term care facility
        - Frailty
        - Advanced age
        - Other underlying conditions that a healthcare provider determines might increase severe RSV risk

- ACIP recommends that co-administration with other adult vaccines during the same visit is ACCEPTABLE, including seasonal influenza, COVID-19, pneumococcal, Td/Tdap and recombinant zoster
    - Data is only available for administration with flu vaccines, and it is possible co-administration with other vaccines might increase local or systemic reactogenicity (e.g., MRESVIA with mRNA COVID-19 vaccine, or AREXVY with SHINGRIX)

References

1. Respiratory syncytial virus vaccine (MRESVIA) [prescribing information]. Moderna: May 2024. Accessed 7/29/24
2. FDA summary basis for regulatory action, MRESVIA. 5/31/24. Accessed 7/29/24.
3. ACIP meeting materials. June 2024 meeting. ACIP June 26-28, 2024, Presentation Slides | Immunization Practices | CDC
4. Britton A, Roper L, Kotton C, et al. Use of respiratory syncytial virus vaccines in adults aged ≥ 60 years: Updated recommendations of the Advisory Committee on Immunization Practices – United States, 2024. *MMWR* 2024;73(32):696-702
5. Wilson E, Goswami J, Baqui PA., et al. Efficacy and safety of an mRNA-based RSV prefusion F vaccine in older adults. *NEJM* 2024;389:2233
6. Melgar M, Britton A, Roper L, et al. Use of respiratory syncytial virus vaccines in older adults: Recommendations of the Advisory Committee on Immunization Practices – United States, 2023. *MMWR* 2023;72(29):793-801.